GUIDELINES FOR MONITORING HEPATOTOXICITY OF ANTITUBERCULAR THERAPY

An official statement of the American Thoracic Society (ATS) Board of Directors concerning TB drug hepatotoxicity was published on October 15, 2006. This important review and the extensive use of potentially hepatotoxic antitubercular drugs prompted the development of these guidelines.

Potentially hepatotoxic medications in the primary treatment of TB include isoniazid, rifampin and pyrazinamide.

The decision concerning the use of isoniazid or any of the antitubercular drugs is the clinic physician's responsibility. Their indication for and use in latent tuberculosis infection (LTBI) involves risk assessment for determining the likelihood of developing tuberculosis versus the patients' risks of the drug itself. Guidelines for this decision can be found in the Core Curriculum on Tuberculosis and other official statements. However, the use of these drugs in the treatment of active tuberculosis largely revolves around drug toxicity to the individual patient.

The following guidelines are recommended any time one or a combination of these antitubercular drugs is used:

1. Baseline liver function tests should be obtained before beginning therapy in all individuals.
2. Standard questionnaire should be obtained relating to the patient's medical condition, including the existence of liver disease such as hepatitis or jaundice, the use of alcohol, or the existence of HIV.
3. Only a one month supply of the drug(s) should be dispensed and monthly nurse assessment for compliance and for symptoms of toxicity should be carried out. Anorexia, nausea, vomiting, darkened urine, jaundice, malaise, elevated temperature, and abdominal tenderness should alert one to the possibility of hepatotoxicity and medications should be stopped immediately, liver function tests obtained, and medication not to be restarted until re-evaluation by the physician.
4. All patients with active TB disease should be treated by directly observed therapy (DOT). The nurse should be assessing the patient for compliance and for symptoms of toxicity during the DOT process (as per #3 above).
5. Liver function tests should be obtained monthly on all individuals. More frequent liver function testing may be performed if the clinic physician and/or clinic nurse feels it is appropriate due to other factors. Assessment of liver blood profiles should trigger the following responses:

    A. **Elevation of LDH alone** without any other liver function test abnormalities does not warrant cessation of medication.
    B. Any elevation of bilirubin and/or alkaline phosphatase requires cessation of medication and consultation with the clinical physician.
    C. Minor elevations in ALT, AST, and GGT up to three times the upper limits of normal does not warrant cessation of medication. The medication should be continued unless there are clinical indications to do otherwise. Consultation with the clinician should be obtained. If these enzymatic levels are between three and five times the upper limits of normal then medication should be withheld and consultation with the clinic physician should be obtained to determine if further therapy is advised. Levels of these enzymes

above five times the upper limits of normal require consideration of discontinuing medication or selection of alternative therapy, depending upon the patient's disease status.

6. Patient education is extremely important and should include printed material. The patient should categorically be told to immediately stop medication for symptoms such as nausea, vomiting, abdominal discomfort, fatigue, or fever and to consult the clinic for further evaluation. The assessment should include a nurse's evaluation and liver function assessment.

   Prior to beginning and any time during therapy, abnormal liver profiles are to be sent to the patient's primary health care provider as well as to the clinic physician. The patient should inform his/her health care provider of any antitubercular medications prescribed.

28 November 2006

Signed: D Gaziano

Dominic J. Gaziano, M.D.
Medical Director
Tuberculosis Control Program